REMARKS

The Official Action dated June 19, 2001 has been carefully considered. Accordingly, the changes presented herewith, taken with the following remarks, are believed sufficient to place the present application in condition for allowance. Reconsideration is respectfully requested.

By the present Amendment, claims 1 and 2 are amended to clarify that a metal salt is added prior to peptide isolation. Support for the amendment of claims 1 and 2 is found in Examples 3-5. A Version With Markings Showing Changes Made is attached. Claim 20 is added. Support for claim 20 is found on page 2, lines 28-30. It is believed that these changes do not involve any introduction of new matter, whereby entry is believed to be in order and is respectfully requested.

Claims 1-3, 5-8 and 11-19 were rejected under 35 U.S.C. §102(b) as being anticipated by Christensen (WO 96/02570A1). The Examiner asserted that Christensen discloses a method for the production of recombinant peptides by teaching that the addition of sulfite salts, preferably at a pH of 7, converts trisulfide bridges into disulfide bridges.

As will be set forth below, Applicants submit that the methods defined by present claims 1-3, 5-8 and 11-19 are not anticipated by Christensen. Accordingly, this rejection is traversed and reconsideration is respectfully requested.

Claim 1 recites a method for the production of recombinant peptides with a low amount of trisulfides. The method comprises fermenting cells to produce the recombinant peptides, wherein a metal salt is added during or after the fermentation step, prior to peptide isolation. Claim 2 recites a method for the reduction of the amount of trisulfides in the production of recombinant peptides. The method comprises fermenting cells to produce recombinant peptides, wherein a metal salt is added during or after fermentation, prior to peptide isolation.

Anticipation under 35 U.S.C. §102(b) requires the disclosure in a single prior art reference of each element of the claims under consideration, *Alco Standard Corp. v. TVA*, 1 U.S.P.Q.2d 1337, 1341 (Fed. Cir. 1986). While the Christensen reference teaches the addition of sulfite salts, preferably at a pH of 7, to a hydrophobic derivative of growth hormone to convert formed trisulfide bridges into disulfide bridges of the native form, Applicants find no teaching or suggestion by Christensen of a method wherein a metal salt is added during or after fermentation and prior to peptide isolation, as in claim 1, therefrom to prevent the formation of the trisulfides. Rather, Christensen teaches treatment of isolated growth hormone derivative. Thus, Christensen does not disclose each element of the present claims and therefore does not anticipate these claims.

It is therefore submitted that the methods defined by claims 1-3, 5-8 and 11-19, are not anticipated by Christensen, and the rejection under 35 U.S.C. §102 has been overcome. Reconsideration is respectfully requested.

Claims 1-3, 5-8 and 11-19 were rejected under 35 U.S.C. §103(a) as being unpatentable over Sorensen et al (WO 94/24157), and further in view of Breton et al, *J. Chromatography*, Vol. 709, 1995, pg. 135-146. The Examiner asserted that Sorensen et al teach a method for the production of recombinant peptides and the effect of sulfur atoms in rhGH production, while Breton et al teach a method for reducing trisulfide to disulfide and its effect on the production of recombinant protein.

However, as will be set forth below, Applicants submit that the methods defined by claims 1-3, 5-8 and 11-19 are nonobvious over and patentably distinguishable from the cited combination of references. Accordingly, this rejection is traversed and reconsideration is respectfully requested.

The method for the production of recombinant peptides with a low amount of trisulfides of claim 1 and the method for the reduction of the amount of trisulfides in the

production of recombinant peptides of claim 2 are discussed above. Neither method is rendered obvious by the cited combination of references.

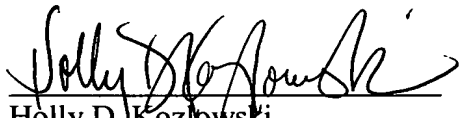
Particularly, Sorensen et al disclose a method for detecting and treating a polypeptide, particularly a hydrophobic derivative of growth hormone. More particularly, the Sorensen et al method treats the growth hormone with a Mercapto compound to convert trisulfides already formed in isolated peptide. However, Applicants find no teaching, suggestion or reference by Sorensen et al of a method of adding a metal salt prior to peptide isolation as in claim 1, thereby to prevent the formation of trisulfides.

The deficiencies of Sorensen et al are not resolved by Brenton et al. Breton et al disclose a method for reducing trisulfides to disulfides already formed in an isolated protein. However, Applicants find no teaching, suggestion or reference by Breton et al of a method of adding a metal salt prior to peptide isolation.

References relied upon to support a rejection under 35 U.S.C. §103 must provide an enabling disclosure, i.e., they must place the claimed invention in the possession of the public, In re Payne, 203 U.S.P.Q. 245 (CCPA 1979). In view of the failure of Sorensen et al, in view of Breton et al to teach, suggest or recognize a method of adding a metal salt prior to peptide isolation, the combination of these references does not provide an enabling disclosure of the present invention, and therefore does not support a rejection under 35 U.S.C. §103. It is therefore submitted that the rejection under 35 U.S.C. §103 has been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the objections and rejections under 35 U.S.C. §§102 and 103 and places the present application in condition for allowance. Reconsideration and an early allowance are requested.

Respectfully submitted,



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Version With Markings Showing Changes Made

Claims 1 and 2 are amended to read as follows:

1. (Twice Amended) Method for the production of recombinant peptides with a low amount of trisulfides, comprising fermenting cells to produce the recombinant peptides, wherein a metal [of] salt is added during or after the fermentation step, prior to peptide isolation.

2. (Twice Amended) Method for the reduction of the amount of trisulfides in the production of recombinant peptides comprising fermenting cells to produce recombinant peptides, wherein a metal salt is added during or after fermentation, prior to peptide isolation.